

**MODULATION OF EXCITABLE TISSUE FUNCTION  
BY PERIPHERALLY ADMINISTERED ERYTHROPOEITIN**

This application claims priority under 35 U.S.C. §119(e) to U.S. provisional patent Application No. 60/129,131 filed April 13, 1999, the entire contents of which is incorporated herein by reference in its entirety.

**1. FIELD OF THE INVENTION**

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The present invention is directed to the use of peripherally administered erythropoietin and other erythropoietin receptor activity modulators or EPO-activated receptor modulators to positively affect excitable tissue function. This includes the protection of excitable tissue, such as neuronal and cardiac tissue, from neurotoxins, hypoxia, and other adverse stimuli, and the enhancement of excitable tissue function, such as for facilitating learning and memory. The present invention is further drawn to methods for transport of substances across endothelial cell barriers by association with an erythropoietin molecule, erythropoietin receptor activity modulator or other EPO-activated receptor modulators.

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**2. BACKGROUND OF THE INVENTION**

Various acute and chronic conditions and diseases originate from excitable tissue damage and dysfunction brought about by external and internal stimuli. Such stimuli include lack of adequate oxygenation or glucose, neurotoxins, consequences of aging, infectious agents, and trauma. For example, excitable tissue may be subjected to damage as a consequence of seizures and chronic seizure disorders, convulsions, epilepsy, stroke, Alzheimer's disease, Parkinson's disease, central nervous system injury, hypoxia, cerebral palsy, brain or spinal cord trauma, AIDS dementia and other forms of dementia, age-related loss of cognitive function, memory loss, amyotrophic lateral sclerosis, multiple sclerosis, hypotension, cardiac arrest, neuronal loss, smoke inhalation and carbon monoxide poisoning.

It is widely understood that decreases in energy supply available to the brain, such as glucose or oxygen, results in a profound impairment of brain function, including cognition. Many (but not all) neurons in the central nervous system are easily damaged